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SPECIFICATION

FOR

PATENT APPLICATION

IN

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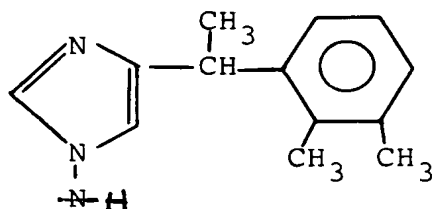
FARMOS-YHTYMA OY

"METHOD OF BRINGING ABOUT SEDATION AND/OR ANALGESIA
IN A MAMMAL"

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This invention relates to sedative and analgesic agents useful in the veterinary field.

4-[(α -Methyl)-2,3-dimethyl-benzyl]₄imidazole of the formula



(I)

TOO20X

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has been disclosed in the European Patent Publication No. 72615 as an antihypertensive agent. 4-(2,3-Dimethylbenzyl)-imidazole, or detomidine, is a known sedative and analgesic agent useful in horses and cattle. Detomidine is used in veterinary medicine as a pharmacological restraint to keep the animal sedated before investigation, treatment and difficult medical operations. Even a small surgical operation cannot be carried without the use of a sedative agent. The effect of detomidine in horses and cattle has been described in the literature, e.g. O. Vainio: "Detomidine hydrochloride, a novel imidazole-type sedative-analgesic". Pharmacologie et Toxicologie Veterinaires, INRA Publ. Paris, 1982, Les Colloques de l'INRA, No. 8. There is also a great need for sedative-analgesic agents as pharmacological restraints in the treatment of dogs, cats and other small animals, but no useful effect was, however, observed.

We have now surprisingly found that the above-mentioned detomidine analogue, 4-[(α -methyl)-2,3-dimethylbenzyl]₄imidazole (compound (I)) is very effective as a sedative and analgesic in the treatment of small animals, especially dogs and cats, but also, e.g., guinea ^{pigs} and rabbits.

Intramuscular or intravenous administration of this compound at a dose of 10 to 160 μ g/kg (in dogs and cats) or 200 to 400

2

ug/kg (in guinea pigs and rabbits) induces a sedative effect
which appears in 2 to 10 minutes after intramuscular (i.m.)
administration or in 0.5 to 1 min. after intravenous (i.v.)
administration. Both the strength and the duration of the
5 effects are clearly dose dependant. Higher doses have a
hypnotic effect during which the animals do not react to
external stimuli such as sounds, pain etc. The duration of
the effect is about 1 to 4 hours in dogs and 0.5 to 2 hours
in cats. Sedation is accompanied by an analgesic effect,
10 especially at higher doses. This compound possesses both a
sedative and an analgesic effect, which are clearly superior
to those of xylazine, which is a known compound commonly used
as sedative in the treatment of small animals. The following
test data illustrate the invention. The tests were carried
15 out using six beagle dogs per group. The study was carried
out using a cross-over-design. Different doses of compound
(I) were given i.m. or i.v.. The reactions observed were
compared to those obtained by xylazine.

Table 1: Reaction to sounds

dose, µg/kg	compound (I)						xylazine			
	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.
results (number of dogs):										
normal reaction	-	1	-	-	-	-	6	4	2	2
weak reaction	3	-	-	-	1	1	-	2	3	4
no reaction	3	5	6	6	5	5	-	-	1	-
total number of dogs	6	6	6	6	6	6	6	6	6	6

Table 2: Duration of the sedation

dose, µg/kg	compound (I)						xylazine			
	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.
duration:										
0 - 15 min	-	-	-	-	-	-	4	2	2	1
15 - 30 min	2	2	-	-	-	-	2	4	3	4
30 - 60 min	4	4	3	4	1	2	-	-	1	1
1 - 2 h	-	-	3	2	3	3	-	-	-	-
> 2 h	-	-	-	-	2	1	-	-	-	-
total number of dogs	6	6	6	6	6	6	6	6	6	6

Table 3: First signs of sedation

	mean, min		variation, min	
	i.m.	i.v.	i.m.	i.v.
compound (I), 40 µg/kg	5	0.7	3 - 10	0.5 - 1
compound (I), 80 "	3	0.6	2 - 6	0.5 - 1
compound (I), 160 "	2	0.5	2 - 3	0.5 - 0.5
xylazine, 1500 µg/kg	4	2	2 - 8	0.5 - 10
xylazine, 3000 "	2	0.5	2 - 3	0.5 - 0.5

Table 4: Evaluation of the sedative effect

T0050X

	compound (I)						xylazine			
dosage, µg/kg	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.
no activity	-	-	-	-	-	-	-	-	-	-
some activity	-	1	-	-	-	-	6	6	2	3
good activity	6	5	6	6	6	6	-	-	4	3
total no of dogs	6	6	6	6	6	6	6	6	6	6

Table 5: Evaluation of the analgesic effect

T0051X

	compound (I)						xylazine			
dosage, µg/kg	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.
no activity	-	-	-	-	-	-	-	-	-	-
some activity	1	3	-	-	-	-	6	6	4	5
good activity	5	3	6	6	6	6	-	-	2	1
total no of dogs	6	6	6	6	6	6	6	6	6	6

Table 6: The position of the animal during the maximum effect

T0052X

	compound (I)						xylazine			
dosage, µg/kg	40		80		160		1500		3000	
administration	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.	i.m.	i.v.
position:										
standing	-	-	-	-	-	-	1	-	-	-
able to get up easily	-	-	-	-	-	-	4	4	2	2
able to get up with difficulty	3	3	1	-	-	1	1	2	4	4
not able to get up	3	3	5	6	6	5	-	-	-	-
total no of dogs	6	6	6	6	6	6	6	6	6	6

CM We claim:

5